## Remarks

### Priority

The Office Action asserts that there is not at least one common named inventor between the current application and the parent applications. The instant application is a continuation in part of U.S. Ser. No. 09/980,845 filed on November 15, 2001, which is the U.S. national stage of PCT/US00/21340, filed August 4, 2000, which claims the benefit of U.S. Ser. No. 60/147,551, filed August 6, 1999. All of these applications, along with the instant application, have inventor Jeffery D. Hillman in common. As such, the priority claim is correct.

### Oath/Declaration

A new declaration is attached.

### Rejection of Claims 1-7 and 9-12 Under 35 U.S.C. §112, first paragraph

Claims 1-7 and 9-12 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse the rejection.

The Office asserts that the specification does not provide enablement for antibodies that is not produced from infected animals or humans.

Under 35 U. S. C. §112, all that is required is that the specification describe the invention in such terms as to enable a person skilled in the art to make and use the invention. The test of enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. *In re Wands*, 858 F.2d

731 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. §2164.01. "The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard of the nature of the invention and the state of the art." *In re Wa*nds, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (citing *Ansul Co. v. Uniroyal, Inc.*, 169 U.S.P.Q. 759, 762-63 (2d Cir. 1971). "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.*

One of ordinary skill in the art could make and use the invention without undue experimentation. Claim 1 recites **adsorbing antibodies against antigens that are expressed by the microbe *in vivo* and *in vitro*** with cells or cellular extracts of the microbe that have been grown *in vitro*. The claim specifies that the antibodies are "against" (i.e., specific for) antigens that are expressed by the microbe *in vivo* and *in vitro*. The source of the antibodies is immaterial. The antibodies may comprise sera from one or more hosts infected with, or previously infected with the microbe. However, the antibodies can also be, for example, a mixture of previously identified antibodies that are specific for antigens expressed by the microbe *in vivo* and *in vitro*. For example, the specification teaches that:

> Antibodies of the invention are antibody molecules that specifically and stably bind to a microbial polypeptide of the invention or fragment thereof. An antibody of the invention can be a polyclonal antibody, a monoclonal antibody, a single chain antibody (scFv), or a part of an antibody. Parts of antibodies include Fab and $F(ab)_2$ fragments. Antibodies can be made *in vivo* in suitable laboratory animals or *in vitro* using recombinant DNA techniques. Means for preparing and

characterizing antibodies are well know in the art. See page 30, lines 10-15.

The claimed method will work as long as the antibodies are specific for antigens that are expressed by the microbe *in vivo* and *in vitro.* Of course, a sample could also comprise only antibodies that are specific for antigens that are expressed by the microbe *in vivo* or antibodies specific for antigens that are expressed by the microbe *in vitro* only. One of skill in the art could make and use the claimed invention without undue experimentation.

Applicants respectfully request withdrawal of the rejection.

**Rejection of Claims 1-12 Under 35 U.S.C. §112, second paragraph**

Claims 1-12 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. Applicants respectfully traverse the rejection.

The Office asserts that the claims are vague and indefinite because the term "unadsorbed" may mean antibodies that have not yet been adsorbed with microbes and may also mean "the non-subtracted" antibodies. It is unclear to Applicant what meaning the Office is attributing to the term "non-subtracted" antibodies. However, the term is used in the claims and in the specification to mean an antibody that is not specifically bound to an antigen. For example, the specification teaches:

> Antibodies that bind to antigens that are produced during *in vitro* propagation of the microbe of interest are eliminated from the sample of antibodies against antigens that are expressed by the microbe *in vivo.* The antibodies that are reactive with antigens produced *in vitro* can be removed from the sample by, for example, adsorbtion. Preferably, a sample containing antibodies against antigens that are expressed by the microbe *in vivo* and *in vitro,* such as a serum sample of an infected host,

> are contacted with *in vitro* grown whole cells, cell extracts or both of the microbe, or whole cells, extracts of whole cells, or both of cells that are infected with the microbe of interest, *e.g.* a prokaryotic or eukaryotic cell infected with a virus or parasite.
>
> All or substantially all of the antibodies in the antibody sample whose corresponding antigens are derived from *in vitro* grown microbes will bind to these antigens to form immune complexes. However, antibodies directed against antigens that are specifically expressed during the *in vivo* infectious process will remain uncomplexed since their corresponding antigens are not present in the *in vivo* grown cells and/or cell extracts. The adsorbtion step can be performed by, for example, contacting the antibody sample with whole cells and/or cell extracts that are immobilized on a solid support, such as a nitrocellulose membrane. *See,* Brady & Daphtary, *J. Infect. Dis.* 158:965-972 (1988). Optionally, the whole cell and/or cell extract sample can be denatured before use to expose additional immunoreactive epitopes. Several successive adsorbtions can be performed using the same or different adsorbtion methodologies.
>
> After the adsorbtion step or steps, unbound antibodies are separated from the antibody-antigen complexes. After elimination of antibodies reactive with microbial antigens expressed *in vitro*, the sample will comprise antibodies produced in response to antigens specifically expressed *in vivo*. *See,* specification, page 15, line 18 through page 16, line 18.

One of ordinary skill in the art, given the specification, would understand that the "unadsorbed antibodies" of the claims refer to antibodies that are not bound to an antigen in an immunocomplex.

A claim is definite when those skilled in the art would understand what is claimed when the claim is read in light of the specification. *See, Orthokinetics Inc. v. Safety Travel Chairs Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986). Claims must be sufficiently precise to permit a potential competitor to determine whether or not they are infringing. *See, Exxon Research and Eng'g Co. v. United States*, 265 F.3d 1371, 1376, 60 U.S.P.Q.2d 1272, 1276 (Fed. Cir. 2001).

The Office asserts that there is uncertain antecedent basis in claim 4 and its dependant claims for the term "an antigen." The Office asserts that the relationship between "an antigen" in claim 4 to the "antigens" in claim 1 is unclear. Initially, claim 4 references to "an antigen." According to the basic rules of claim construction, the use of "an antigen" in claim 4 instead of "the antigen" means that "an antigen" of claim 4 does not refer to "the antigens" of claim 1. Claim 1 recites "a method of identifying a polynucleotide of a microbe that is expressed *in vivo*". Claim 4 recites that the polynucleotide encodes an antigen. One of skill in the art, given the specification, would understand that what the term "an antigen" means in claim 4.

The Office asserts that the claims are indefinite because the term "phage" has insufficient antecedent basis. Claim 1 has been amended to provide antecedent basis for the term "phage."

The claims are definite and applicant respectfully requests withdrawal of the rejection.

**Rejection of Claims 1-12 Under 35 U.S.C. §103(a)**

Claims 1-12 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over WO 01/11081; U.S. Pat. No. 6,048,527; and U.S. Pat. Appl. No. 2004/0247611. Applicants respectfully traverse the rejection.

WO01/11081 names the following inventors: Progulske-Fox, Handfield, Brady, and Hillman. The subject matter of WO01/11081 is assigned to iviGene Corporation. *See*, attached assignment (00-505B). The instant application names Hillman as the sole inventor. Inventor Hillman has assigned the instant application to iviGene Corp. *See*, attached

assignment (00-505I). At the time the instant invention was made the subject matter and claimed invention were owned by the same person (iviGene Corp.) or subject to an obligation of assignment to the same person. Therefore, under 103(c), WO01/11081 does not preclude patentability under §103(a).

U.S. Pat. Appl. No. 2004/0247611 was filed on February 19, 2004. The instant application was filed on March 6, 2002. U.S. Pat. Appl. No. 2004/0247611 is not prior art and therefore cannot be cited in an obviousness rejection.

Applicants respectfully request withdrawal of the rejection.

**Rejection of Claims 1-12 Under 35 U.S.C. §103(a)**

Claims 1-12 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Handfield *et al.*, U.S. Pat. No. 6,048,527 ("the '527 patent"), and U.S. Pat. Appl. No. 2004/0247611. Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the references, when combined must teach or suggest all the claim limitations. *See*, M.P.E.P. §2143.

There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There must be some reason, suggestion, or motivation found in the cited references whereby a person of ordinary skill in the field of the

invention would make the substitutions required. That knowledge cannot come from the applicants' disclosure of the invention itself. *Diversitech Corp. v. Century Steps, Inc.*, 7 U.S.P.Q.2d 1315,1318 (Fed. Cir. 1988); *In re Geiger*, 2 U.S.P.Q.2d 1276, 1278 (Fed. Cir. 1987); *Interconnect Planning Corp. v. Feil*, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985).

As described above, U.S. Pat. Appl. No. 2004/0247611 is not prior art. Therefore, motivation and reasonable expectation of success allegedly provided by U.S. Pat. Appl. No. 2004/0247611 cannot be considered.

The Office appears to have engaged in a hindsight analysis of obviousness. Combining prior art references without evidence of a suggestion, teaching, or motivation to combine the references takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability, which is the essence of hindsight. *See, e.g.*, *Interconnect Planning Corp. v. Feil* , 774 F.2d 1132, 1138, 227 U.S.P.Q. 543, 547 (Fed. Cir. 1985). The suggestion or motivation must come from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. *See, Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 U.S.P.Q.2d 1626 (Fed. Cir. 1996); *Para-Ordinance Mfg. v. SGS Imports Intern., Inc.*, 73 F.3d 1085, 1088, 37 U.S.P.Q.2d 1237, 1240 (Fed. Cir. 1995. Broad conclusory statements about the teachings of multiple references are not evidence. *See, e.g., McElmurry v. Arkansas Power & Light Co.*, 995 F.2d 1576, 1578, 27 U.S.P.Q. 2d 1129, 1131 (Fed. Cir. 1993).

The '527 patent teaches functionally active antibodies directed against MenB PS derivatives, wherein the antibodies do not cross-react, or are minimally cross-reactive, with host tissues. The Office suggests that the '527 patent teaches the specific antibody

selection of polynucleotides encoding antigens borne on phage display libraries. However, neither Handfield nor the '527 patent teaches or suggests the use of probing a phage display library of a microbe's DNA or RNA with the unadsorbed antibodies of step (b) of claim 1; wherein the step of probing a phage display library comprises:

(i) immobilizing the unadsorbed antibodies on a solid support;

(ii) adding the phage display library of the microbe's DNA or RNA to the solid support;

(iii) washing unbound phage from the solid support; and

(iv) recovering phage that are bound to the solid support;

such that a polynucleotide of the microbe that is expressed *in vivo* is isolated and identified.

Additionally, there is no motivation or teaching to combine the teachings of the '527 patent, regarding functionally active antibodies directed against menB PS derivatives wherein the antibodies do not cross react or are minimally cross reactive with host tissues, with Handfield, regarding methods of identifying *in vivo* expressed antigens.

Applicants respectfully request withdrawal of the rejection.

**Rejection of Claims 1-12 Under 35 U.S.C. §103(a)**

Claims 1-12 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Hautefort *et al.*, the '527 patent, and U.S. Pat. Appl. No. 2004/0247611. Applicants respectfully traverse the rejection.

As described above, U.S. Pat. Appl. No. 2004/0247611 is not prior art and cannot be considered in this rejection. Neither Hautefort nor the '527 patent (discussed above) teach or suggest the claimed methods. Additionally, there is no motivation or teaching to

combine the teachings of the '527 patent, regarding functionally active antibodies directed against menB PS derivatives wherein the antibodies do not cross react or are minimally cross reactive with host tissues, with Handfield, regarding methods of identifying *in vivo* expressed antigens.

Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

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